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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,018	03/08/2006	Mikio Shoji	023312-0122	4736

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,018	SHOJI ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,35 and 43* is/are pending in the application.

4a) Of the above claim(s) *43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claim 23 has been amended and claims 25-34 and 36-42 have been canceled as requested in the amendment filed on 06 April 2010. Following the amendment, claims 23, 24, 35 and 43 are pending in the instant application,

Claim 43 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on 10 July 2008 and 20 November 2008.

Claims 23, 24 and 35 are under examination in the instant office action.

Claim Rejections Withdrawn

Any outstanding rejection of claims 25-34 and 36-42 is hereby withdrawn as moot in response to the cancellation of said claims.

Applicant's arguments and declaration filed 06 April 2010, with respect to the rejection of claim 35 under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement have been fully considered and are persuasive. The declaration is sufficient to demonstrate that applicants have complied with the deposit rules (see MPEP §2411.05 and 37 C.F.R. § 1.809(d)). The rejection of claim 35 under 35 U.S.C. 112, first paragraph has been withdrawn.

Remaining issues are set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 24 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schenk et al. (WO 00/72880A2, published 07 December 2000;

citation N on PTO-892 dated 13 November 2009), in view of Suzuki et al. (5,750,349; issued 12 May 1998; citation A1 from IDS dated 08 March 2006).

Schenk (WO 00/72880A2) discloses methods of treating a disease characterized by amyloid deposits of amyloid-beta (Aβ) in the brain of a patient (including Alzheimer's disease, Down's syndrome and cognitive impairment in human patients), comprising either active immunization methods or passive immunization methods. Active immunization is practiced via administration to a subject of an effective amount of an immunogenic Aβ peptide, including Aβ 35-42, such that antibodies to the peptide are generated in the subject (see e.g. p.27, lines 26-31). Passive immunization is practiced via administration to a subject of an effective amount of an antibody to an Aβ peptide (see e.g. p.32, lines 20-27). Schenk teaches the desirability of administration of an effective dosage of antibodies that specifically bind to a component of an amyloid deposit in the patient (p.2, lines 28-33; p.11, line 24). Some of the antibodies bind to the long form of Aβ (i.e. Aβ 1-42 or Aβ 1-43), while not binding to a short form of Aβ (i.e. Aβ 1-38 or SEQ ID NO: 1, Aβ 1-39 or SEQ ID NO: 2, Aβ 1-40 or SEQ ID NO: 3 or Aβ 1-41)(see p.33, lines 24-26), thus implying the suitability of C-terminal antibodies to Aβ 1-42 or Aβ 1-43 for treatment of Alzheimer's disease. Schenk does not explicitly teach administration of an antibody that specifically reacts with a partial peptide at the C-terminal region of Aβ but does not recognize a partial peptide of SEQ ID NO: 8, as claimed.

However, the Suzuki patent teaches the specific monoclonal antibodies which are administered in the instant method claims. It is noted that Suzuki's SEQ ID NOs: 1,

2, 3, 4, 5, 6, 7, 8 and 9 are identical to the instant SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8 and 9, respectively. Thus, Suzuki teaches the antibody of claims 23 and 24 at col.4, lines 50-55. The patent teaches antibodies to derivatives which meet the limitations recited by claim 23 at col.5, lines 62-65. The antibody of claim 35 (i.e. BC-05a) is taught at col.7, lines 1-2. The patent also teaches that the antibodies of the invention are useful for the development of preventative or therapeutic compositions for Alzheimer's disease (abstract). Suzuki does not explicitly teach administration of the antibodies for methods of treating Alzheimer's disease.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the methods of Schenk as taught by Suzuki et al. to yield predictable results. As evidenced by the Schenk document, the artisan of ordinary skill would have known that an antibody specific to the long form of Aβ (i.e. Aβ 1-42 or Aβ 1-43) would be useful in treating Alzheimer's disease and/or cognitive impairment. As evidenced by Suzuki et al., the artisan of ordinary skill would have known that the C-terminal antibodies (which are specific to the "long form" of Aβ) disclosed therein could be used in methods of developing treatments for Alzheimer's disease. Furthermore, it would have been reasonable to predict that the antibodies of Suzuki could be successfully used in the methods of treating Alzheimer's disease and/or cognitive impairment taught by Schenk because Schenk suggests that such antibodies would be suitable. That is, given that Schenk teaches that raising antibodies against the long form of Aβ would be desirable and teaches that a preferred immunogenic peptide is Aβ 35-42, and given that Suzuki et al. teach such C-terminal

antibodies against the long form of Aβ, the artisan of ordinary skill would have found it obvious to try to use Suzuki's antibodies in Schenk's treatment methods. Therefore, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify Schenk's treatment methods by administering Suzuki's antibodies to yield predictable results. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense (see KSR International Co. v. Teleflex Inc. (KSR), 550 U.S. ____, 82 USPQ2d 1385 (2007).

In the reply filed on 06 April 2010, applicants assert that Schenk teaches away from combining Schenk and Suzuki. Applicants assert that Schenk's antibodies, which are not directed to the C-terminus region of Aβ, showed treatment effects such as reduced Aβ levels in the cortex, hippocampus and cerebellum in animals treated and that the monoclonal antibody 21F12, which is directed to the C-terminus region of Aβ, did not show such treatment effects. Thus, applicants assert that the artisan of ordinary skill would understand that Aβ-C-terminus-region-specific antibody could not be used for reducing Aβ levels in the cortex, hippocampus and cerebellum and thus could not be used for treating Alzheimer's disease. Applicants conclude that the artisan of ordinary skill would not use Suzuki's antibody, which is directed to the C-terminus region of Aβ, instead of Schenk's antibody, which is not directed to the C-terminus region of Aβ, for treating Alzheimer's disease.

Applicants' arguments have been fully considered and are not found persuasive. Applicants' argument that administration of Schenk's monoclonal antibody 21F12 did not show treatment effects such as reduced Aβ levels in the cortex, hippocampus and cerebellum in animals is not entirely accurate. Although 21F12 showed more modest effects than some of the other antibodies tested, it still resulted in reduced Aβ levels in the cortex, hippocampus and cerebellum in animals treated (see Tables 13-15). Thus, Schenk's teaching of treatment with a C-terminal antibody does not teach away from the claimed invention. MPEP §2123 (II) states that "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi,* 440 F.2d 442, 169 USPQ 423 (CCPA 1971). 'A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use.' *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)." Additionally, MPEP §2123 (I) states that "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied,* 493 U.S. 975 (1989). See also >*Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component);< Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed

invention. 'The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.)." Indeed, as set forth above, Schenk teaches that some of the antibodies for passive immunization bind to the long form of Aβ (i.e. Aβ 1-42 or Aβ 1-43), while not binding to a short form of Aβ (i.e. Aβ 1-39, Aβ 1-40 or Aβ 1-41)(see p.33, lines 24-26), thus implying the suitability of C-terminal antibodies to Aβ 1-42 or Aβ 1-43 for treatment of Alzheimer's disease. This is hardly a teaching away from treatment with C-terminal antibodies to Aβ.

In the reply filed on 06 April 2010, applicants assert that the present invention demonstrates unexpected results because the present specification shows advantageous effects of the present invention. Applicants assert that for example, administration of BC-05a, which is directed to the C-terminus region of Aβ, resulted in removal and amelioration of the deposition of cerebral Aβ. Applicants refer to p.24, lines 18-25 of the present specification, which states that "any change in the soluble Aβ x-40 level in the brain was not observed but a reducing tendency of the insoluble Aβx-40 level was observed. The Aβx-42 level in the brain was significantly increased for the soluble fraction but a reducing tendency for the insoluble fraction was observed." Thus, applicants assert that the presently claimed antibodies were able to preferentially remove the type of Aβ that is associated with Alzheimer disease and that this is unexpected, especially in view of Schenk.

Applicants' arguments have been fully considered and are not found persuasive. That the instant specification shows advantageous effects of the present invention does not mean that the results are unexpected. Applicants point to data in the specification

which demonstrate that BC-05a reduced insoluble Aβ levels more efficiently than soluble levels. This is not commensurate in scope with the claimed invention as the claimed invention merely recites administration of antibodies for treatment of Alzheimer's disease and related disorders. Moreover, as set forth above, Schenk teaches the desirability of administration of an effective dosage of antibodies that specifically bind to a component of an amyloid deposit in the patient, i.e. those that selectively bind insoluble Aβ (p.2, lines 28-33; p.11, line 24). Schenk teaches that in some methods, antibodies are therapeutically effective by clearing already established amyloid deposits (made up of insoluble Aβ) and enables the artisan to screen for antibodies with plaque clearing activity (see e.g., p.3, lines 16-18 and p.34, line 1 – p.35, line 15). Thus, applicants' alleged unexpected results are actually expected from the disclosures of the prior art of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.
/G.E./

Gregory S. Emch
Patent Examiner
Art Unit 1649
22 June 2010

/Daniel E Kolker/
Primary Examiner, Art Unit 1649
July 1, 2010